MARKED-UP COPY OF AMENDED CLAIMS:

1. (Thrice Amended) A taste masked formulation which rapidly releases in the stomach of a patient comprising:

a drug-containing core;

a taste masking layer composed of a material which is generally insoluble in saliva at a neutral to basic pH and completely soluble in saliva at a pH of less than about 6.5; and

a spacing layer surrounding said core and substantially completely sequestering said core from said taste masking layer and being capable of rapidly exposing said core when exposed in the stomach of a patient; ~~wherein said spacing layer comprises ethyl cellulose, methyl cellulose, hydroxypropyl cellulose, hydroxy propyl methyl cellulose, polyalkylene glycols, polyalkylene oxides, sugars, sugar alcohols, shellacs, acrylics, or mixtures thereof,~~ said taste masking layer preventing exposure of said spacing layer in the mouth of a patient for a period of at least about 20 seconds after being placed into the mouth and being capable of rapidly exposing said spacing layer when in the stomach of a patient; wherein the coated drug-containing core generally has a diameter of no larger than 1,500 microns.

14. (Thrice Amended) A dosage form intended for direct oral administration, comprising:

an effective amount of at least one drug, said drug present in the cores of coated particles, said cores including a taste masking layer composed of a material which is generally insoluble in saliva at a neutral to basic pH and completely soluble in saliva at a pH of less than about 6.5; and

a spacing layer surrounding said core and substantially completely sequestering said core from said taste masking layer and being capable of rapidly exposing said core when exposed in the stomach of a patient; ~~wherein said spacing layer comprises ethyl cellulose, methyl cellulose, hydroxypropyl cellulose, hydroxy propyl methyl cellulose, polyalkylene glycols, polyalkylene oxides, sugars, sugar alcohols, shellacs, acrylics, or mixtures thereof,~~ said taste masking layer preventing exposure of said spacing layer in the mouth of a patient for a period of at least about 20 seconds after being placed into the mouth

and being capable of rapidly exposing said spacing layer when in the stomach of a patient; and

at least one pharmaceutically acceptable excipient provided in an amount of between greater than zero and less than 100%, based on the weight of the finished dosage form; wherein the coated drug-containing core generally has a diameter of no larger than 1,500 microns.

REMARKS

Claims 1, 4-18, and 21 were pending. Claims 1 and 14 are amended. Claims 22-25 are added. Upon entry of this Amendment, claims 1, 4-18, 21-25 will be under examination.

Support for the amendments to claims 1 and 14 can be found, *inter alia*, on page 12, lines 21-22 of the original specification. Support for the new claims 22-25 can be found *inter alia*, on page 12, lines 20-23 of the original specification. Applicants contend that the amendments to claims 1 and 14 the addition of new claims 22-25 are fully supported by the original specification and do not raise any issue of new matter. Therefore, entry of this Amendment is respectfully requested.

REJECTION UNDER 35 U.S.C § 102(b)

Claims 1, 4, 5, 14, and 21 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Kais *et al.*, U.S. Patent No. 5,516,524 ("Kais").

In order to expedite the prosecution of this application, without conceding to the correctness of the Office Action's position, applicants have amended claims 1 and 14 to recite that the coated drug-containing core has a diameter which is generally no larger than 1500 microns. While it is possible that some percentage of the coated drug cores will have a diameter which is above 1500 microns, the intention of this initially is to make it clear that the preponderance of the cores will have a diameter of 1500 microns or less. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

Applicants contend that Kais does not disclose the use of a material which is generally insoluble in saliva as a neutral to basic pH and completely soluble in saliva at a pH of less than 6.5 as the outer-layer. Kais also does not disclose the use of a coated drug-containing core having a diameter of no larger than 1500 microns. Therefore, Kais does not disclose each and every element of claims 1, 4, 5, 14 and 21, as amended, and does not anticipate these claims under the standard of MPEP § 2131.

REJECTIONS UNDER 35 U.S.C §103(a)

Claims 1, 4 to 18 and 21 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Kais as applied to claims 1, 4, 5, 14 and 21. Applicants respectfully traverse this rejection as Kais does not teach or suggest the subject matter of claims 1, 4-18 and 21, as amended.

Applicants respectfully point out that the Office Action fails to establish a *prime facie* case of obviousness under the standard of M.P.E.P. § 2142 which states that:

> to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure.

The Office Action does not meet at least the first and third requirements. Specifically, Kais discloses laxative composition containing bulk fiber and coated dioctyl sulfosuccinate. Kais does not provide a teaching suggestion or motivation to a skilled artisan on how to obtain the claimed taste masked formulation and, in particular, one wherein the coated drug-containing core has a diameter of no larger than 1,500 microns and one that employs an outer-layer coating material that is soluble in acidic pH and insoluble in neutral and basic pH. The "suggestion or motivation" criteria must be satisfied from the disclosure of the prior art reference or from the knowledge of persons skilled in the art, (see M.P.E.P. 2143.01) not by the use of hindsight in view of the present application (emphasis added).

In this case, Kais does not teach or disclose "all the claim limitations." Specifically, Kais does not disclose the taste masked formulation wherein the coated drug-containing core has a diameter of no larger than 1,500 microns. Therefore, the Office Action fails to satisfy the third criteria for establishing a *prime facie* case of obviousness under the M.P.E.P. 2143.01.

Moreover, without looking at the disclosure of the present application, a person of skill in the art would not know from Kais how to obtain the claimed formulation having the advantages described in the specification, *e.g.* the formulation "disintegrates rapidly in the mouth to form a suspension of particles which will, once they clear the mouth, release their contents so as not to significantly interfere with the normal bioavailability of the active ingredient" (page 13, lines 10-15 of the specification) and "in one aspect, the present invention requires the formation of a rapidly disintegrable tablet. That means that the tablet

will disintegrate in the mouth of the patient in less than 90 seconds" (page 13, lines 24-26 of the specification). Therefore, the Office Action does not satisfy the first criteria for establishing a *prime facie* case of obviousness under M.P.E.P. 2143.01.

Indeed, for the reasons stated below, Kais actually teaches away from the present invention. Kais generically teaches a host of potential coating materials including, amongst many others, pH sensitive materials, and states that these coating materials can be used in any order for any layer. However, in its only example of the use of a double coating system, employing a pH sensitive material, the pH sensitive material is used as barrier or inner coating layer. Plastersizers are used as the second or outer protective coating. This arrangement provided the stated advantages of Kais, as recited in column 5, lines 22-25, namely that "the coating can also be chosen so that it remains largely intact through the stomach, thereby avoiding gastric disturbances which are commonly associated with use of dioctyl sulfosuccinate as a medicinal drug." Therefore, Kais' only direct teaching; the only help or direction it provides a person of ordinary skill in the art in ascertaining which of the thousands of possible combinations of coatings and layering encompassed by its broad teaching, is directly away from the claimed invention.

As noted in answer to prior office actions, the present invention utilizes a pH sensitive coating on its outer-layer which is relatively impervious to bases but completely rapidly removed by exposure to acids. Such an outer protective coating would provide absolutely no benefit to Kais in terms of the prior stated objective of intestinal delivery. It is however, effective in protecting the drug while the drug resides in the mouth and delivery in the stomach. Moreover, using a material as described in Kais as the outer protective layer in accordance with the present invention would be equally disastrous. Such a material is designed to be impervious to acid, but not necessarily base, would provide none of the desired taste masking.

With the claimed objectives in mind, one reading Kais would not realize that one set of formulations broadly falling within its disclosure would be effective and another would be completely ineffective. And indeed, to the extent that any direction is provided at all, it directs one to a formulation which will not work and which is opposite to the claimed formulation in terms of the construction and content of the respective layers. Since a teaching

away is a strong indicia of nonobviousness, applicants respectfully submit that the claimed invention is not obvious.

Moreover, the foregoing illustrates that the Patent Office's rejection is an impermissible "obvious to try" rejection. As stated *In re O'Farrell*:

> The admonition that "obvious to try" is not the standard under § 103 has been directed mainly at two kinds of error. In some cases, what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. In others, what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it.

7 U.S.P.Q. 2d 1673, 1681 at 1681 (Fed. Cir. 1988) (citations omitted).

It is clear that this rejection is the first of these. Kais sets out multiple parameters and choices providing no indication as to how to select among them so as to arrive at the claimed invention.

With regard to the Office Action's assertion that "solubility characteristics are inherent to the specific coating," applicants respectfully point out that the Board of Patent Appeals and Interference held in *Ex parte Schricker*, 56 USPQ2d 1723 (Bd. Pat. App. & Int., 2000) that "inherency and obviousness are somewhat like oil and water — they do not mix well." The Board further stated that "when an examiner relies on inherency, it is incumbent on the examiner to point to the 'page and line' of the prior art which justifies an inherency theory." In this case, the Office Action does not points to the "page and line" of Kais to justify an inherency theory on solubility. The Office Action also does not points to the "page and line" of Kais to justify an inherency theory on fast disintegration of the claimed formulation.

Therefore, claims 1, 4-18 and 21, as amended, are nonobvious over Kais. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

CONCLUSION

In view of the amendments and the remarks, the present application is in condition for allowance. Entry of this Amendment, and favorable action in the form of a Notice of Allowance with respect to claims 1, 4-18 and 21-25 are respectfully requested.

If any fee is required, the examiner is authorized to charge such fee to our Deposit Account No. 12-1095.

Respectfully submitted,

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